UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,746	03/03/2004	Franz Paul Armbruster	0756-0124P	2900

2292 7590 11/10/2010

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
HAQ, SHAFIQUL	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
11/10/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/790,746	ARMBRUSTER ET AL.	
	Examiner	Art Unit	
	SHAFIQUL HAQ	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7-9 and 11-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7-9 and 11-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/10/2010 has been entered.

Status of claims

2. Claims 1, 3-4, 7-9 and 11-18 are pending and examined on merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 3 and 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: separation of 1α, 25-hydroxy vitamin D for the measurement of the amount of 1α, 25-hydroxy vitamin D in a sample. Separation of 1α, 25-hydroxy vitamin D is a critical steps for measuring the amount of 1α, 25-hydroxy vitamin D in a sample. See the specification (page 34), wherein sample includes plasma sample and separation of 1α, 25-hydroxy vitamin D from

25-OH-vitamin D_3 is described to be an essential step in the measurement of the amount of 1α, 25-hydroxy vitamin D in a sample.

6. With regard to claims 1 and 15, it is unclear as to whether antibody that specifically binds to 1α, 25-hydroxy vitamin D is encompassed in the definition of "vitamin D binding protein" or not because as claimed in the amended claim 15, it seems Applicants are intended to include antibody that specifically binds to 1α, 25-hydroxy vitamin D by the term "vitamin D binding protein". Further, it is vague and indefinite as to what chemical or physical properties or structure (s) is/are intended to be described for 1α, 25-hydroxy vitamin D by the term "**as** the vitamin D binding protein"?

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 3 and 11-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for measuring the amount of separated (isolated) 1α, 25-hydroxy vitamin D metabolite, does not reasonably provide enablement for measuring the amount of 1α, 25-hydroxy vitamin D metabolite in a sample in the presence of 25-hydroxy vitamin D metabolite in the sample (i.e. in the presence of both the metabolites in a sample) without the separation (isolation) of 1α, 25-hydroxy vitamin D metabolite from the sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to use the invention commensurate in scope with these claims. The method as claimed measures 25-hydroxy vitamin D metabolite and/or 1α, 25-hydroxy vitamin D metabolite in a sample by competitive protein binding assay using a vitamin D derivative of formula (I) as a competitor. However, in a sample (note that serum is encompassed by the term "sample") where the 1α, 25-hydroxy vitamin D metabolite is very low (e.g. human serum where 25-hydroxy vitamin D metabolite to 1α, 25-hydroxy vitamin D metabolite is 1000:1; see paragraph 2, page 34 of specification), the displacement of vitamin D derivative of formula (I) from the vitamin D binding protein would be mainly due to 25-hydroxy vitamin D metabolite and thus the displacement cannot be correlated to the amount of 1α, 25-hydroxy vitamin D metabolite in the serum sample. See second paragraph (page 34) of specification and page 7 of Applicants' argument (10/10/07), which describe separation of 1α, 25-hydroxy vitamin D from sample is an essential step for the detection of 1α, 25-hydroxy vitamin D in serum by competitive protein binding assay and thus the method as claimed is not enabled for measuring 1α, 25-hydroxy vitamin D metabolite in the presence of 25 hydroxy vitamin D metabolite and 1α, 25-hydroxy vitamin D metabolite in the sample. The term "vitamin D binding protein" as described in the specification is limited to Gc-globulin (See first line on page 2, line 29 on page 6 and last line on page 5, which state "binding protein such as antibody or vitamin D binding protein"), which is not described in the specification capable of differentiating 1α, 25-hydroxy vitamin D over 25-hydroxy vitamin D so that 1α, 25-

hydroxy vitamin D can be specifically measured in the presence of 25-hydroxy vitamin D in a serum sample.

A claim which omits matter disclosed to be essential to the invention as described in the specification or in other statements of record may be rejected under 35 U.S.C. 112, first paragraph, as not enabling. In re Mayhew, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). See also MPEP § 2164.08(c).

9. Claim 1, 3 and 11-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 as recited claims detection of 25-hydroxy vitamin D in a sample with either one of the 25-hydroxy vitamin D biotin compound (i.e. when Y=H) or 1α, 25-hydroxy vitamin D biotin compound (when Y=OH) as competitor or detection of 1α, 25-hydroxy vitamin D with either one of the 25-hydroxy vitamin D biotin compound (i.e. when Y=H) or 1α, 25-hydroxy vitamin D biotin compound (when Y=OH) as competitor. However, the specification does not teach using tracer 25-hydroxy vitamin D biotin compound (i.e. when Y=H) for measuring of 1α, 25-hydroxy vitamin D (see Example 9, wherein tracer compound 1α, 25-hydroxy vitamin D biotin is used for detection of 1α, 25-hydroxy vitamin D in a sample) and there in no disclosure in the specification for measurement of 1α, 25-hydroxy vitamin D in a sample with the tracer 25-hydroxy vitamin D biotin as claimed in claim 1. Similarly, the specification

does not teach using tracer 1α, 25-hydroxy vitamin D compound (i.e. when Y=OH) for measuring of 25-hydroxy vitamin D in a sample (see Example 3, wherein tracer compound 25-hydroxy vitamin D biotin is used for detection of 25-hydroxy vitamin D in a sample) and there in no disclosure in the specification for measurement of 25-hydroxy vitamin D in a sample with the tracer 1α, 25-hydroxy vitamin D as claimed in claim 1.

The MPEP states that the purpose of written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject mater later claimed and the specification does not clearly describe or suggest in the specification for an accurate quantitative determination (measurement) of 1α, 25-hydroxy vitamin D in a sample with the 25-hydroxy vitamin D-biotin tracer as encompassed by claim 1 and similarly the specification does not clearly describe or suggest in the specification for an accurate quantitative determination (measurement) of 25-hydroxy vitamin D in a sample with the 1α, 25-hydroxy vitamin D-biotin tracer as encompassed by claim 1.

Accordingly, it is deemed that the specification fails to provide adequate written description and clear guidance for compounds encompassed by "linker" and does not reasonable convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

10. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was

not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 16 recites "measuring the displacement of a vitamin D derivative of formula (I) from an antibody that specifically binds 1α, 25-hydroxy vitamin D, wherein a displacement efficiency of approximately 1 is obtained by using vitamin D derivative of formula (I)". However, in the specification, displacement efficiency of approximately 1 for vitamin D derivation of formula (I) with antibody that specifically binds 1α, 25-hydroxy vitamin D has not been disclosed or described anywhere in the specification. The displacement efficiency as described in the specification (Example 11 and Fig.15) is displacement efficiency of vitamin D derivative of formula (I) with respect to vitamin D binding protein (Gc-globulin. See first line on page 2, line 29 on page 6 and last line on page 5, which state "binding protein such as antibody or vitamin D binding protein"), not with antibody that specifically binds 1α, 25-hydroxy vitamin D.

New or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement. See, e.g., In re Lukach, 442 F.2d 967, 169 USPQ 795 (CCPA 1971).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 3-4, 7-8 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holick et al. (WO 97/24127).

Holick teaches methods for detecting the presence of vitamin D analogs and their metabolites in a sample using labeled vitamin D compounds (i.e. vitamin D derivative) in the assay method (see field of invention). The vitamin D metabolites includes , 1,25 dihydroxy vitamin D3, 25 hydroxy vitamin D2 etc. (page 1, lines 12-25 and page 5, lines 10-14). The labeled vitamin D derivative of Holick (see compounds B and C of example 2 and 3 of pages 14-15) reads on the compound of the formula of claim 1 when R represents a 25-hydroxy side-group of vitamin D3, Y=H, A= functional group coupled via a spacer group, which can be bound by a protein with high affinity (see definition of A in lines 9-16 of specification wherein A can be biotin). Holick discloses a method in which labeled vitamin D derivative is first allowed to bind to a protein or an antibody capable of binding to the vitamin D derivative and which is attached to a solid support. Sample containing vitamin D metabolite is then added to effect displacement of the labeled compound from said protein and Holick discloses that preferred protein is vitamin D binding protein (DBP) (see pages 11-12). Holick discloses different immunoassay methods (page 10, lines 21-25 and page 12, lines 9-11) and solid phase support including dextran, agarose, polystyrene and microtitration plate (page 11, lines 27-29) and the solid phase can be beads, plates or tubes (page 10, lines 15-16).

Holick discloses displacement of vitamin D derivatives from vitamin D binding protein (i.e. competitive detection) but remain silent about displacement efficiency with the vitamin D derivative. However as described above, the labeled vitamin D derivatives of Holick are very similar or the same as the vitamin D derivatives of formula (I) of instant application and they are expected to show similar properties (e.g. similar displacement properties from vitamin D binding proteins). PRODUCT, MPEP §2112 states "[Where] the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established." In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)(emphasis added).

With regard to Kit of claims 4 and 7-8, Holick discloses that the labeled compounds are ideally suited for the preparation of a kit and the kit may contain labeled vitamin D derivative, vitamin D binding protein and avidin coated beads, plates etc. (page 10, lines 9-20). Holick does not recite standardized quantity of vitamin D derivatives but standardized quantity of components in a kit composition is obvious to one of ordinary skill in the art.

13. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Holick et al. (WO 97/24127) as described above and further in view of DeLuca et al. (US 5,064,770).

See above teaching for Holick et al.

Holick et al disclose kit comprising solid phase (e.g. beads) and vitamin D derivative but differ from the instant application in failing to disclose magnetic microparticle as solid phase.

DeLuca et al. in a binding assay to determine 1, 25-dihydroxy vitamin D receptor disclose using magnetic particle for anchoring binding molecules to the particle.

Since the use of magnetic particle is very common in the field of immunoassay and magnetic particle has been disclosed for detection of vitamin D binding protein (DeLuca et al.), it would be obvious to one of ordinary skill in the art at the time the invention is made to include magnetic particle in the method of Holick et al. for detection of vitamin D metabolites involving vitamin D binding protein with a reasonable expectation of success.

14. Claims 15, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holick *et al* (WO 97/24127) as described above for claims 1, 3-4, 7-8 and 11 and further in view of admitted prior art (Mawer *et al* 1985: see page 33, lines 25-27).

As described above, Holick *et al* teach a method in which labeled vitamin D derivative is first allowed to bind to a protein or an antibody capable of binding to the vitamin D derivative and which is attached to a solid support. Holick *et al* teach that any antibody which is capable of binding vitamin D, its metabolite or analog can be used (page 12, lines 5-6).

Therefore, given the fact that antibody against 1,25 dihydroxy vitamin D is known in the art (admitted prior art) that binds to a vitamin D analog, it would be obvious to

one of ordinary skill in the art to consider using the antibody against 1,25 dihydroxy vitamin D for attaching to solid phase with the expectation of detection of 1,25 dihydroxy vitamin D in a sample using the vitamin D biotin tracer (see the traces in examples 3 and 5) because Holick *et al* teach providing solid phase support having immobilized thereon a protein or an antibody which is capable of binding to labeled compound of the invention and Holick *et al* teach that any antibody which is capable of binding vitamin D, its metabolite or analog can be used and further, Holick *et al* is concerned with the detection of 1,25 dihydroxy vitamin D in a sample (Page 5, lines 10-14). Moreover, once a method process in known, providing the components in a kit for convenience would be obvious to one of ordinary skill in the art.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1, 3-4, 7-8 and 11-13 are again rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,787,660 in view of Holick et al. (WO 97/24127. (Note that the method claims were not restricted out in the parent application i.e. there was not restriction requirement on the method claims in parent application).

Claims 1-5 of US patent discloses 25-OH vitamin D derivatives which reads on the vitamin D derivative of formula (I). See claims 2 and 5, wherein A can be selected from biotin.

The claims of US patent '660 do not teach using the derivatives in competitive immunoassays.

Holick teaches methods for detecting the presence of vitamin D analogs and their metabolites in a sample using labeled vitamin D compounds (i.e. vitamin D derivative) in the assay method (see field of invention). The vitamin D metabolites includes , 1,25 dihydroxy vitamin D3, 25 hydroxy vitamin D2 etc. (page 1, lines 12-25 and page 5, lines 10-14) Holick discloses a method in which labeled vitamin D derivative is first allowed to bind to a protein capable of binding to the vitamin D derivative and which is attached to a solid support. Sample containing vitamin D metabolite is then added to effect displacement of the labeled compound from said protein and Holick discloses that preferred protein is vitamin D binding protein (DBP) (see pages 11-12). Holick discloses different immunoassay methods (page 10, lines 21-25 and page 12, lines 9-11) and solid phase support including dextran, agarose,

polystyrene and microtitration plate (page 11, lines 27-29) and the solid phase can be beads, plates or tubes (page 10, lines 15-16).

Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made to include the 25-OH derivatives of vitamin D in the competitive immunoassay method of Holick with the expectation of optimization and improving the detection sensitivity of 25-OH vitamin D metabolite and 1, 25-dihydroxy vitamin D metabolite in a sample with a reasonable expectation of success.

Holick discloses displacement of vitamin D derivatives from vitamin D binding protein (i.e. competitive detection) but remain silent about displacement efficiency with the vitamin D derivative. However as described above, the labeled vitamin D derivatives of Holick are very similar or the same as the vitamin D derivatives of formula (I) of instant application and they are expected to show similar properties (e.g. similar displacement properties from vitamin D binding proteins). PRODUCT, MPEP §2112 states "[Where] the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established." In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)(emphasis added).

With regard to Kit of claims 4, 7-9 and 13, Holick discloses that the labeled compounds are ideally suited for the preparation of a kit and the kit may contain labeled vitamin D derivative, vitamin D binding protein and avidin coated beads, plates etc. (page 10, lines 9-20). Holick does not recite standardized quantity of

vitamin D derivatives but standardized quantity of components in a kit composition is obvious to one of ordinary skill in the art. With regard to length of biotin group and spacing group, the length of spacers and the length of biotin and spacer of at least one of the compounds A-C and D of the reference encompass the length of 0.9 to 1.5 nm of instant application.

Response to Argument

17. Applicant's arguments and amendments filed 5/10/2010 have been fully considered and are persuasive to overcome some of the rejections under 35 USC 112 second paragraph, 35 USC 112 first paragraph and 35 USC 103 (a).

Applicants' arguments and amendments have been fully considered but they are not persuasive to overcome the rejection under 35 USC 112 first paragraph and the rejection under 35 USC 103..

Applicants argued that the compounds of Holick are distinct from vitamin D derivative of formula (I) but did not clearly mention how the structures are distinct. Applicant further argued that Holick's displacement ligands demonstrate a displacement efficiency approximately 1/11 that of the present compounds of formula (I) now claimed.

Applicants' arguments have been fully considered but are not persuasive because labeled vitamin D derivatives of Holick are close structural homolog of vitamin D derivatives of formula (I) of instant application. As for example, compare the compound c (page 15 of the reference) with formula (I). Considering Y=H, and

R=25 hydroxylated side-group of vitamin D, the only difference lies in the alkylene chain in the linker (four CH_2 groups versus five CH_2 groups in between two amide bonds). Therefore, the compound of the reference is a chain homolog of the compound of instant application (differ by only one methylene group) and they are expected to show similar properties {e.g. similar displacement properties at that of formula (I)}. PRODUCT, MPEP §2112 states "[Where] the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established." In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) (emphasis added). Further, homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH_2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977). Since the compound of formula (I) and the compound c of the reference is a chain homolog (differ by only one CH_2 group in the linker), the Examiner maintains that they would exhibit similar displacement properties in a same experimental setup for measurement of displacement efficiency in the absence of any unobviousness or unexpected properties. "Displacement efficiency" and the method to measure the displacement efficiency has not been clearly defined in the specification and Applicants have not shown different properties (i.e. different displacement properties) of the compound of formula (I) from the compound disclosed by Holick

(e.g. compound c of page 15 which is in question) in a same experimental setup (i.e. using the same method process) for measurement of displacement properties. The measurement of displacement for the compound of formula (I) of instant application and the method used in the reference for measuring efficiency of displacement may not be the same and Applicants cannot draw a conclusion form this and assert that they have different displacement efficiency. Further, besides experimental setup, in Holick, displacement experiment was done with human vitamin D binding protein (hDBP) whereas in present application the vitamin D binding protein is from goat serum (See Example 11) and it is known that vitamin D binding protein exists in various isoforms even in the same animal and different isoforms may show different binding characteristics. Moreover, none of the vitamim D derivatives (i.e. compound C or D of Hokic) is included in the displacement efficiency experiment (Example 11) of the instant application to clearly assert with certainty that the compound C and D of Holick *et al* with only one methylene group deference in the linker is distinct from the vitamin D derivative of formula (I) of instant application. With respect to the functional property (displacement from vitamin D binding protein) of the vitamin D derivative, the Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same functional characteristics of the claimed product. They are descriptive and thus would be an inherent property of the claimed composition. In the absence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those

taught by the prior art and to establish patentable differences. See *Ex parte Phillips,* 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray,* 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best,* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). In the instant case, slight modification (only one methylene group in the linker) would result in vitamin D derivative having the claimed formula (I). "Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada,* 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.,* 51 USPQ 2d 1943, 1947 (Fed. Cir.1999). Therefore, merely claiming a new use, new function, or new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best,* 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112.

Applicant argued that when displacement efficiency of the trace is less than 0.1 of DBP then it should be clear to a skilled person that the biotin tracer cannot distinguish between 25-hydroxy vitamin D and 1α, 25-hydroxy vitamin D, notably, when they are present in human serum in a ratio of 1000:1. Applicants further argued that the method of measurement comprises a step of purifying and isolating

1α, 25-hydroxy vitamin D on a column and using an antibody specific for 1α, 25-hydroxy vitamin D to obtain the necessary specificity (see page 10 of the argument).

With regard to above argument, it is noted that the detection as claimed in claim 1 is not limited to detection of 1α, 25-hydroxy vitamin D and the features upon which applicant relies (i.e., detection of only 1α, 25-hydroxy vitamin D in a sample and a step of purifying and isolation 1α, 25-hydroxy vitamin D) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shafiqul Haq/
Primary Examiner, Art Unit 1641